Journal of Traumatic Stress, Vol. 20, No. 4, August 2007, pp. 611–617 (© 2007)

Adult Sexual Abuse is Associated with Elevated Neurohormone Levels Among Women With PTSD Due to Childhood Sexual Abuse

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Posttraumatic stress disorder (PTSD) has been associated with reduced, similar, or increased urinary cortisol levels. The authors identified a factor that might contribute to such variability when they obtained 24-hour urinary neurohormone profiles on 69 women with PTSD due to childhood sexual abuse. Half (n = 35) had subsequently experienced adult sexual abuse (ASA) while the other half (n = 34) had not. The ASA group had significantly elevated urinary cortisol, norepinephrine and dopamine levels in comparison to the non-ASA group. Neither a history of childhood or adult physical abuse nor other variables contributed to this finding. The results suggest that the psychobiological consequences of exposure to the same traumatic event may differ as a result of an interaction between age and the composite history of trauma exposure.

Twenty-four-hour urinary neurohormone levels have been measured in people with posttraumatic stress disorder (PTSD) since the classic studies of Mason and colleagues (Kosten, Mason, Giller, Ostroff, & Harkness, 1987; Mason, Giller, Kosten, Ostroff, & Podd, 1986). Results have generally been consistent for catecholamines and inconsistent for cortisol. There is a large body of evidence suggesting that 24-hour urinary norepinephrine, epinephrine, and dopamine levels are higher among PTSD than among comparison participants (reviewed by Southwick et al., 2007, 1999; Young & Breslau, 2004).

In contrast, different investigators have reported reduced (Yehuda, Teicher Trestman, Levengood, & Siever, 1996), similar (Baker et al., 1999; Kosten, Wahby, Giller,

This research was supported by a grant from the National Institute of Mental Health (RO1-MH52787) and by the National Center for PTSD.

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 DOI: 10.1002/jts.20221

& Mason, 1990; Mason, Wang, Riney, Charney, & Southwick, 2001; Young & Breslau, 2004), or elevated (Lemieux & Coe, 1995; Maes et al., 1998; Pitman & Orr, 1990; Rasmusson et al., 2001) 24-hour urinary cortisol levels in PTSD groups in comparison to controls.

Opinions on how to explain these discrepant urinary cortisol findings include methodological concerns (Yehuda et al., 1996), failure to adequately control for a variety of conditions (such as stress, exercise, smoking, gender, etc.; Rasmusson et al., 2001), the influence of comorbid depression (Young & Breslau, 2004), and intensity of stress at the time of measurement (Mason et al., 2002).

We propose that an interaction between trauma history and developmental factors might contribute to this variability. Trauma history has often varied within cohorts. Many of the aforementioned studies included combinations of individuals who had been traumatized only as children or only as adults or during both periods of their lives. Furthermore, except for pre-/postmenopausal status (Rasmusson et al., 2001; Rasmusson & Friedman, 2002), developmental questions have not been addressed systematically. Could it be that the psychobiological impact of traumatic exposure is different for immature than for mature individuals? Is it possible that a third psychobiological signature emerges when traumatized children are retraumatized as adults?

Although we did not set out to investigate these questions, a serendipitous result emerged when we analyzed baseline data acquired for a randomized clinical trial of cognitive–behavioral therapy for women with PTSD due to childhood sexual abuse (PTSD–CSA; McDonagh et al., 2005) in which we obtained 24-hour urinary neurohormone profiles on 69 women enrolled in the study. Despite the fact that exposure to adult sexual abuse (ASA) was not a selection factor for our PTSD–CSA group, it turned out that approximately half had subsequently experienced ASA whereas the other half had not. To our knowledge, this is the largest cohort of PTSD–CSA women on whom such biological measurements have been obtained and the first cohort from whom it has been possible to study the psychobiological impact of adult sexual trauma on women with PTSD–CSA.

METHOD

Participants

Seventy-three women with PTSD due to CSA participated in a study contrasting the efficacy of cognitive–behavioral therapy, present-centered therapy, and assignment to a wait-listed control group (McDonagh et al., 2005). The women were recruited from the community through a combination of newspaper, radio, television, and poster advertisements. Sexual abuse was defined as unwanted sexual contact that included caressing, fondling, stimulation of the genitalia, coercion to stimulate the perpetrator's genetalia, and/or oral, anal, or vaginal rape. Childhood sexual abuse was defined as some variant of the aforementioned sexual contact with a man 5 or more years older when the woman was under age 16 (Briere & Runtz, 1993). Inclusion criteria were age 18–65, a history of CSA, a diagnosis of current CSA-related PTSD, and at least one clear memory of the childhood sexual abuse. Exclusion criteria were pregnancy, psychotic disorders, current mania, hypomania, dissociative identity disorder, depression requiring immediate psychiatric treatment, current alcohol or drug abuse, alcohol/substance withdrawal within the past 3 months, active suicidal ideation, or two or more parasuicidal behaviors during the past year, and the presence of ongoing interpersonal abuse (e.g., domestic violence, stalking, etc.).

Following written informed consent, the PTSD–CSA participants completed three structured interviews to determine eligibility. The Structured Clinical Interview for DSM-IV (SCID; First, Spitzer, Gibbon, & Williams, 1996) identified Axis I and II psychiatric conditions that were comorbid or precluded participation. The Evaluation of Lifetime Stressors (Krinsley et al., 1994) provided the trauma history. Finally, the Clinician-Administered PTSD Scale (CAPS; Blake et al., 1995; Weathers, Keane, & Davidson, 2001) provided PTSD diagnosis and symptom severity. In addition, participants completed a battery of self-report assessments including the Beck Depression Inventory (BDI; Beck, Steer, & Garbin, 1988) and the 20-item state anxiety portion of the Spielberger

State Trait Anxiety Inventory (STAI; Spielberger, Gorusch, Lushene, Vagg, & Jacobs, 1996). Participant compensation was $50.00 for the baseline assessments.

Procedure

Participants provided urine samples within 10 days of the baseline CAPS assessment. All women were asked to provide two consecutive 24-hour urine collections. A take-home package included detailed written instructions, two or more opaque 3000-mL plastic containers, and urine collection funnels. Once in the laboratory, urine collections were stored in a −20°C freezer. After thawing, total 24-hour volumes were recorded, and several aliquots of each day's collection were decanted and refrozen (−70°C) for subsequent cortisol and creatinine measurements. Additional aliquots were acidified with 6N hydrochloric acid to pH 2.0, then treated with 20 μL/mL EDTA-glutathione solution and refrozen for later catecholamine assay. Analysts of urine samples were blind to all participant information.

Free cortisol excretion levels were determined using a radioimmunoassay (RIA) kit prepared by Incstar (now Diasporin Corporation, Stillwater, MN). An interassay coefficient of variation of 4% was obtained in the laboratory. Urinary levels of epinephrine, norepinephrine, and dopamine were measured using an automated Waters (Waters Corporation, Milford, MA) HPLC (high performance liquid chromatography) system. The urinary catecholamine analysis methods, including sample preparation kits and cation exchange columns, were supplied by Bio-Rad Corporation (Mississauga, Ontario, Canada). The interassay coefficient of variation for epinephrine and norepinephrine measures were 5% and 8% respectively.

Urine collections with less than 0.7g/day creatinine were considered incomplete and invalid and were excluded from further analysis. Assay results were averaged if there were two valid daily collections. If only one collection was valid, its results were recorded. Sixty-nine of the 73 participants provided valid 24-hour urinary neurohormone measurements.

Statistical Analysis

Differences between the ASA and non-ASA groups in continuous demographic and clinical variables were assessed by *t* tests. Group equivalence for categorical variables was assessed by chi-square tests. The four urine variables were included in a one-way multivariate analysis of variance to determine whether there were overall mean differences between the two groups. Follow-up *t* tests were performed on each urine variable, and effect sizes (Cohen's *d*) were computed. Analysis of covariance was used to test the robustness of the group effect while adjusting for demographic, clinical, and physiological factors.

RESULTS

Except for reported adult sexual abuse (35 women with ASA, 34 without), the two groups of women with PTSD–CSA were remarkably similar. There were no significant differences in CAPS total score, age, body mass index, socioeconomic status, level of education, and self-reported use of tobacco, alcohol, antidepressant drugs, or any other medications across a range of psychiatric and medical categories. There were also no differences between groups with respect to rates of childhood or adult physical abuse (see Table 1). However, women experiencing ASA had reliably lower depression (BDI) and anxiety (STAI) scores, and fewer of them reported being married or in a relationship (see Table 1).

The multivariate ANOVA revealed a significant overall group effect, $F(4,\ 64) = 8.03,\ p < .001$. Univariate results indicated that mean daily levels of urinary cortisol, norepinephrine, and dopamine were significantly higher in women with PTSD–CSA and ASA (see Table 2). Urinary epinephrine was also higher in the ASA group, but this difference was not statistically significant. There was no significant difference between groups in mean 24-hour urine volume (ASA = 1551.6 mL vs. no ASA = 1477.2), and no significant group differences in concentrations (μg/mL) were noted for any of the urine variables.

Follow-up analyses examined whether various demographic and clinical variables may have contributed to the

Table 1. Demographic and Clinical Variables for Women With PTSD Due to Child Sexual Abuse With ($n = 35$) and Without ($n = 34$) Adult Sexual Abuse

	No adult sexual abuse		Adult sexual abuse		
	M	*SD*	*M*	*SD*	*t*(67)
Age (years)	41.2	10.1	38.7	9.4	1.04
Body mass index	27.6	6.8	28.0	7.2	0.25
CAPS Total score	70.6	17.8	69.2	12.8	0.38
BDI Total score	21.9	8.7	16.1	7.8	2.93**
STAI Total score	56.8	8.2	51.9	10.6	2.11*
	Count	%	Count	%	χ^2
% Married/living as married	21	61.8	12	34.3	5.22*
% Working	28	82.4	28	80.0	0.06
% Caucasian	32	94.1	34	97.1	0.38
% Income ≤$20k	19	55.9	21	60.0	0.12
% ≤ GED Education	6	17.6	8	22.9	0.29
% Tobacco use	6	17.6	11	31.4	1.76
% Alcohol use	5	14.7	9	25.7	1.29
% Oral contraceptive use[a]	9	26.5	7	20.0	0.40
% Anti-depressant use	11	32.4	13	37.1	0.17
% Child physical abuse	26	76.5	29	82.9	0.44
% Adult physical abuse	18	52.9	25	71.4	2.51

Note. PTSD = posttraumatic stress disorder; CAPS = Clinician Administered PTSD Scale; BDI = Beck Depression Inventory; STAI = State-Trait Anxiety Inventory; GED = general equivalency diploma.
[a]Oral contraceptive or estrogen use.
* $p < .05$. ** $p < .01$.

ASA group difference in the urine variables. Based on the significant group differences in Table 1, BDI score, STAI score, and marital status were added as covariates to the basic model. The significant ASA group difference was not affected for cortisol, norepinephrine, or dopamine. Despite the absence of a significant ASA group difference for the use of tobacco, alcohol, antidepressants, or birth control/estrogen supplements (see Table 1), these variables were also entered as covariates, and the results for ASA group on urine variables remained unchanged. In addition,

Table 2. Urine Variables for Women With PTSD Due to Child Sexual Abuse With ($n = 35$) and Without ($n = 34$) Adult Sexual Abuse

Urine variables	Group	*M*	*SD*	*t*(67)	Effect size (*d*)
Cortisol (μg/day)	No ASA	36.2	9.9	4.34***	1.04
	ASA	52.0	18.8		
Norepinephrine (μg/day)	No ASA	31.1	9.7	3.14**	0.76
	ASA	40.9	15.5		
Epinephrine (μg/day)	No ASA	4.9	2.6	1.17	0.28
	ASA	5.6	2.8		
Dopamine (μg/day)	No ASA	194.6	49.0	4.28***	1.03
	ASA	249.3	56.8		

Note. PTSD = posttraumatic stress disorder; ASA = adult sexual abuse.
** $p < .01$. *** $p < .001$.

the CSA and CSA+ASA groups did not differ significantly, $\chi^2(1, N = 69) = 2.51$, $p < .11$, in the number of women who were premenopausal (<300 days since last period) versus postmenopausal (300 days since last period), nor in the phase of the menstrual cycle (follicular vs. luteal) for those women who were premenopausal (follicular = 0–14 days; luteal = 15–30 days), χ^2 (1, $N = 69$) = 1.54, *ns*. Neither variable changed the neurohormonal differences between the ASA groups when added as a covariate.

We also investigated several rival explanations for the ASA group differences related to trauma history. There was a significantly longer duration, $t(67) = 6.60$ $p < .001$, between the last sexual abuse event and study participation for women with CSA alone ($M = 30.4$ years, $SD = 11.0$) than for those with both CSA and ASA ($M = 14.9$ years, $SD = 8.3$). Yet, when this variable was entered as a covariate, the effect of ASA on the urine variables was unchanged. In addition, a two-way ANOVA was conducted for each of the urine variables with ASA and adult physical abuse (APA) as between-subjects factors. Neither APA nor the interaction of APA and ASA was significant, and these effects did not alter the significant results for ASA.

DISCUSSION

We did not have a non-PTSD CSA comparison group; therefore, we cannot determine whether our observed 24-hour urinary catecholamine and cortisol levels for either of the PTSD-CSA groups were lower, similar, or higher than control values. Therefore, these findings are restricted to a comparison between women with PTSD–CSA who did and did not experience sexual abuse as adults. Nevertheless, we believe that these robust findings should be investigated in future studies comparing PTSD cohorts with nonaffected controls.

The present results indicate that for women with PTSD–CSA, subsequent exposure to ASA is associated with higher catecholamine and cortisol levels. Follow-up analyses indicated that various demographic, clinical, and physiological variables did not contribute to this finding. There was also no significant difference between the two groups with respect to exposure to childhood or adult physical abuse.

As noted above, urinary cortisol in PTSD cohorts has exhibited reduced, similar or elevated levels from one investigation to another. Recruitment of participants for such studies has generally focused on exposure to a specific index trauma (e.g., sexual, combat, motor vehicle accident). In many cases, the index trauma represents only one among several traumatic events to which participants had been exposed. Although descriptive data are often provided regarding nonindex trauma exposure, this information has not been incorporated into data analyses. Our results suggest, at least with respect to urinary cortisol, that it may be useful to focus on an individual's trauma history as a whole, rather than on a specific index trauma that was embedded within a complex history of multiple exposures to the same or to different traumatic experiences. Our results suggest that maturational factors may also play a significant role. For example, the psychobiological consequences of sexual abuse (or other traumas) on neurohormonal function may be different among children and adolescents in contrast to adults. Finally, our results suggest that when PTSD is associated with the sequence of CSA followed by ASA, neurohormonal function may be affected differently than when PTSD is associated with CSA alone.

The CSA+ASA group exhibited a significantly shorter interval between the last episode of sexual abuse and study participation. When recency of sexual trauma was included as a covariate, however, ASA continued to be the only predictor of neurohormonal differences. This may be partially explained by the observation that for some of the younger women in the CSA group, the interval between sexual trauma and collection of 24-hour urine for the present study was shorter than for some of the older women in the CSA+ASA group.

As stated earlier, these findings were not obtained in a hypothesis-driven study designed to detect neurohormonal differences between women with PTSD–CSA with and without ASA. Because of our focus on PTSD—CSA and because of concern about an overly burdensome assessment procedure, we did not apply the same rigor to gathering complete information about variables pertinent

to the present report such as intensity and recency of (childhood and adult) physical abuse.

We have no explanation for the significantly higher BDI and STAI scores exhibited by the CSA alone, in contrast to the CSA+ASA, group. It should be noted, however, that higher BDI scores would be expected to predict higher urinary cortisol levels because depression is associated with hypercortisolism (Carroll, Curtis, Davies, Mendels, & Sugarman, 1976; Maes et al., 1998). Despite this bias in the opposite direction, we found elevated urinary cortisol levels in the CSA+ASA and not in the CSA alone group.

Despite their limitations, we offer these findings because of their potential theoretical and clinical relevance. It is not unusual for sexually (or physically) abused children with PTSD to be later traumatized as adults. Our results suggest that there is an interaction between age and trauma exposure so that the psychobiological consequences of such traumatic exposure may differ as a result. A further question is whether different psychosocial or pharmacological treatments are indicated when PTSD is associated with such different trauma histories. The answers to these questions await further research, as does replication of the current findings.

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